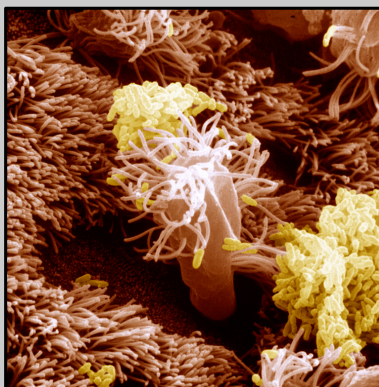
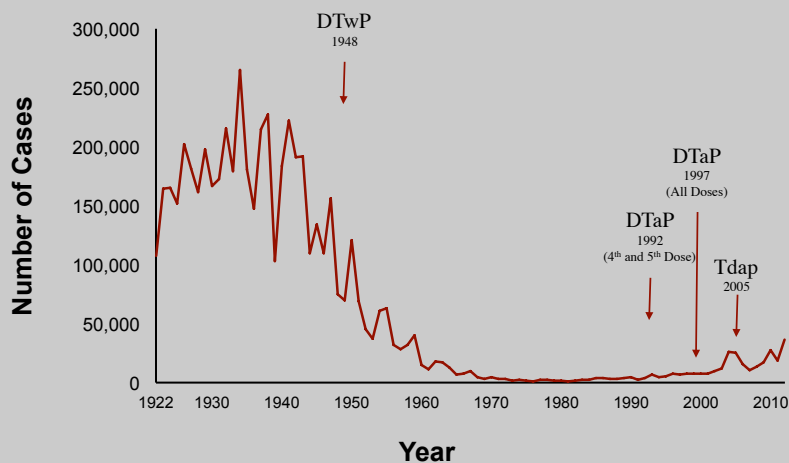


The Baboon Model of Infection with Pertussis

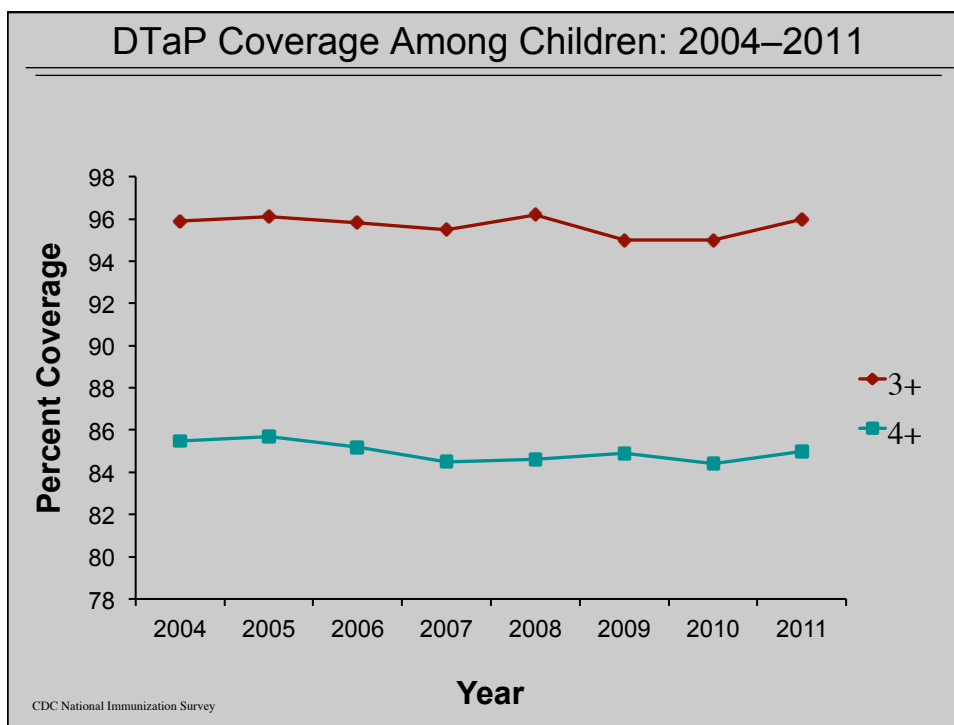
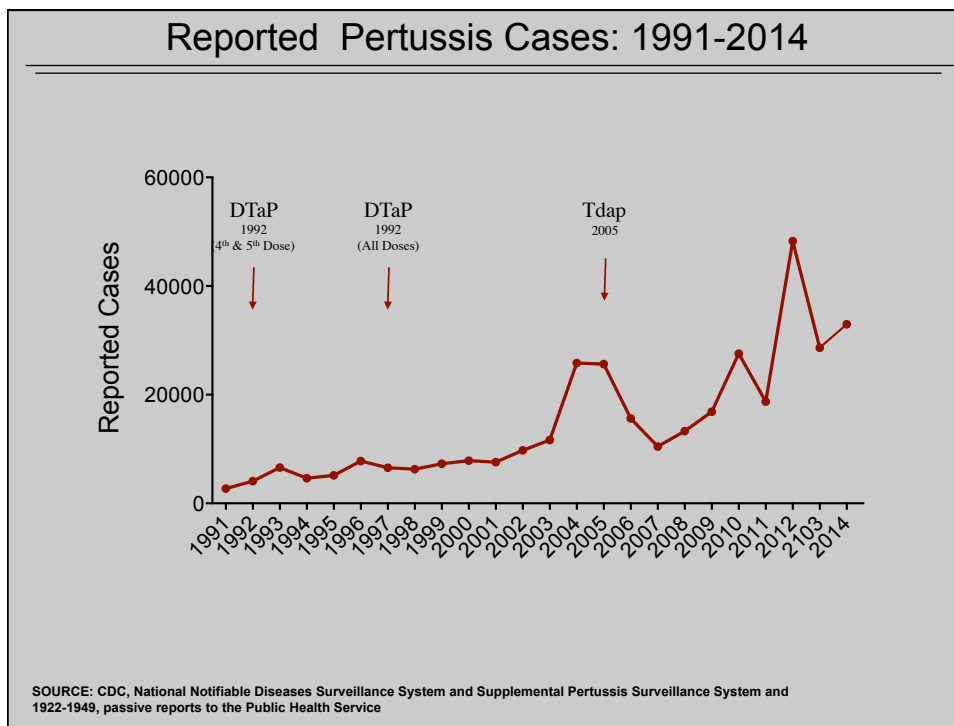


Tod J. Merkel
 Laboratory of Respiratory and Special Pathogens
 CBER/FDA

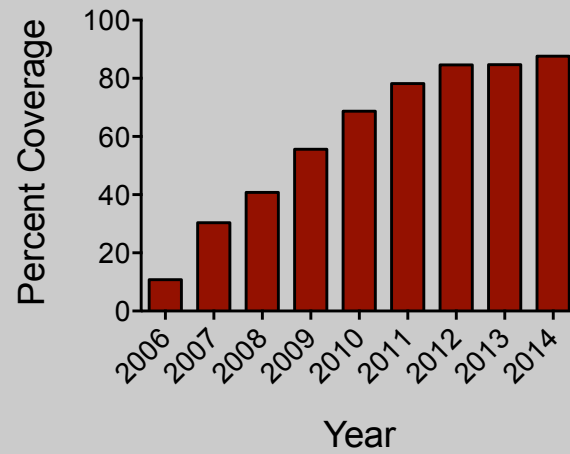
Reported Pertussis Cases: 1922-2014



SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service



Tdap coverage

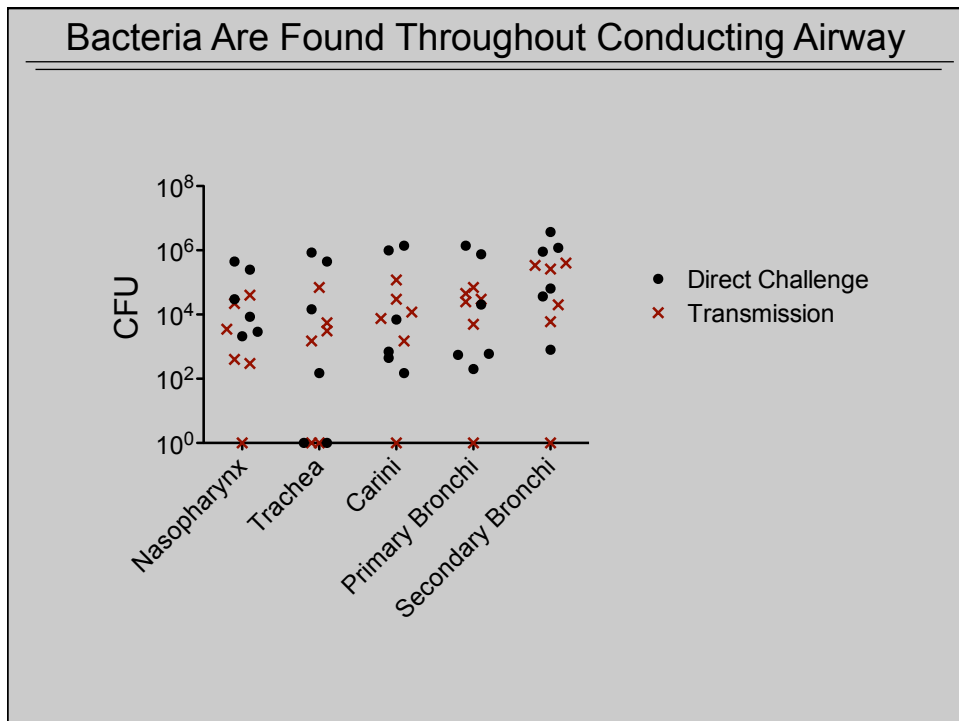
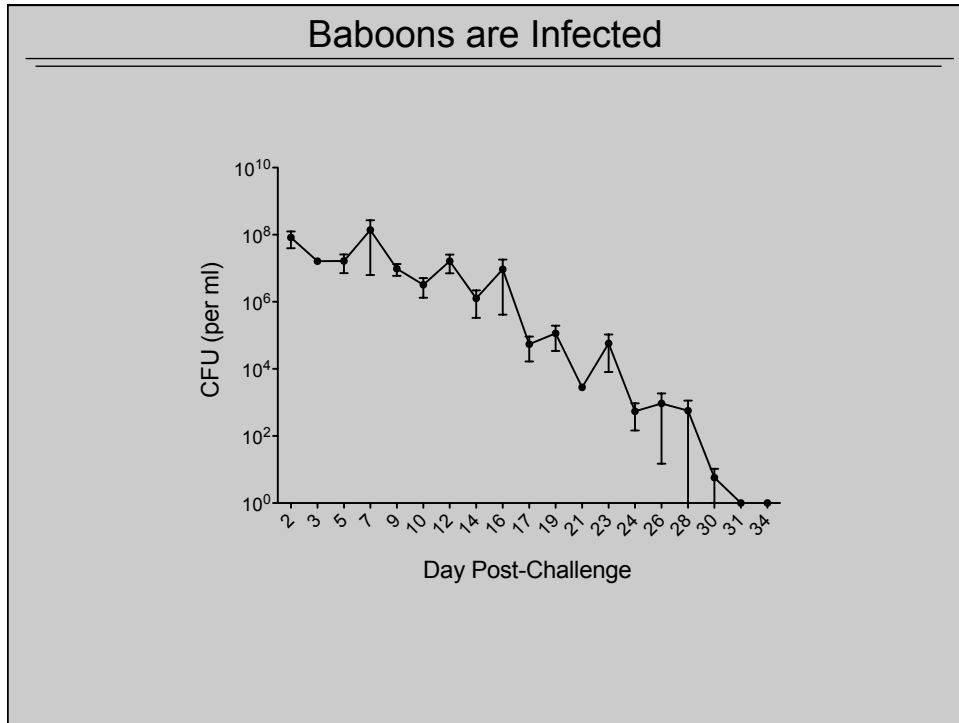


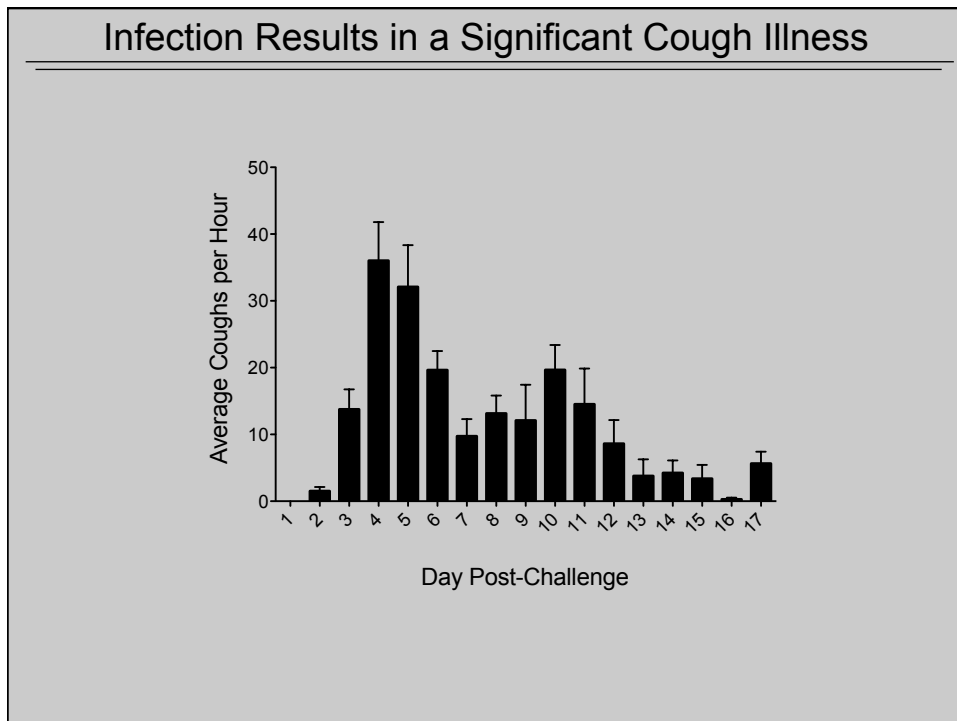
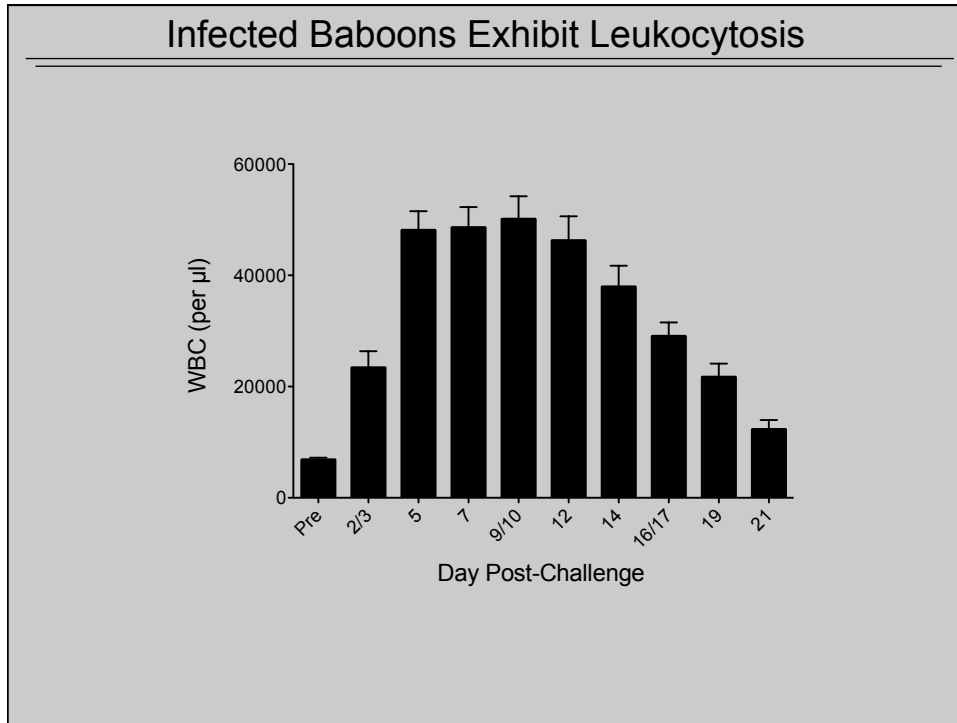
CDC National Immunization Survey

The Baboon Model of Pertussis



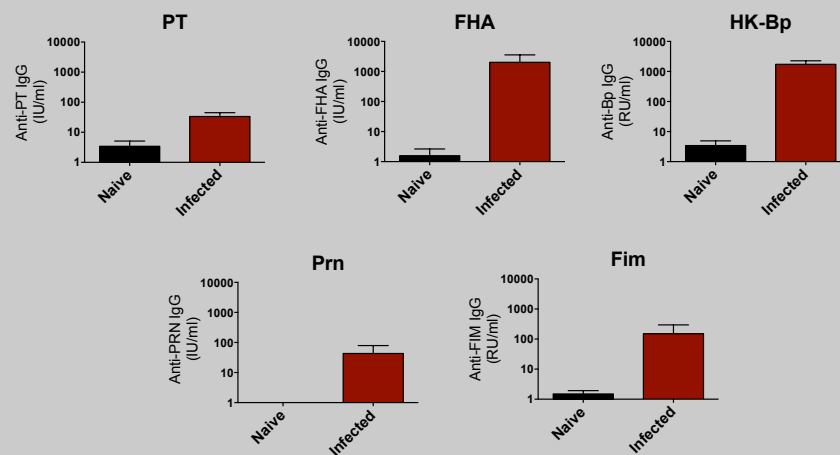
Olive Baboon (*Papio anubis*)

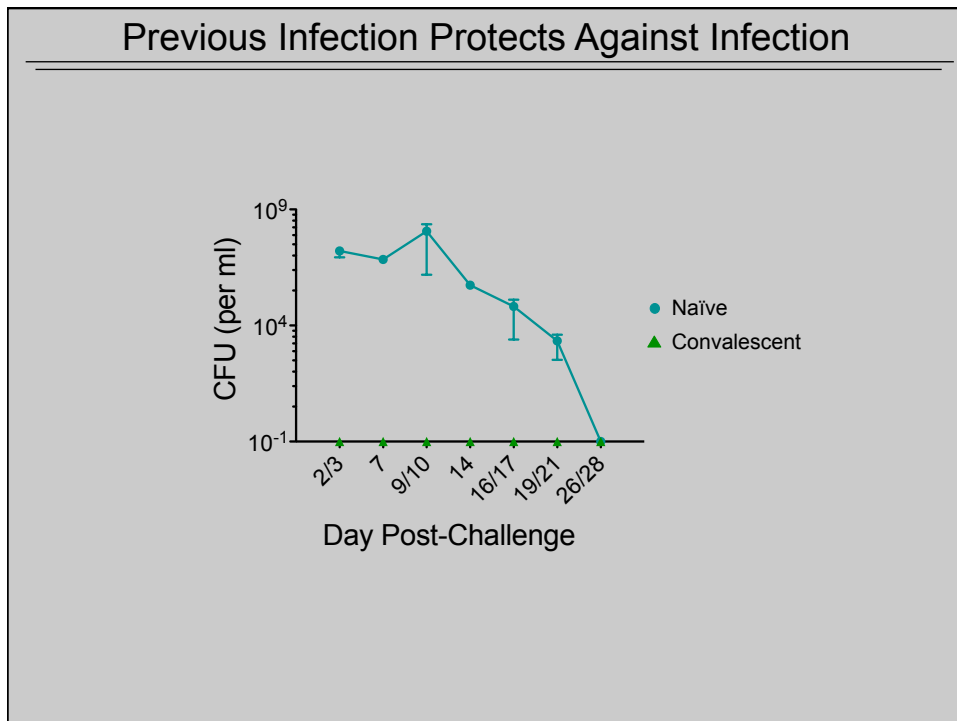
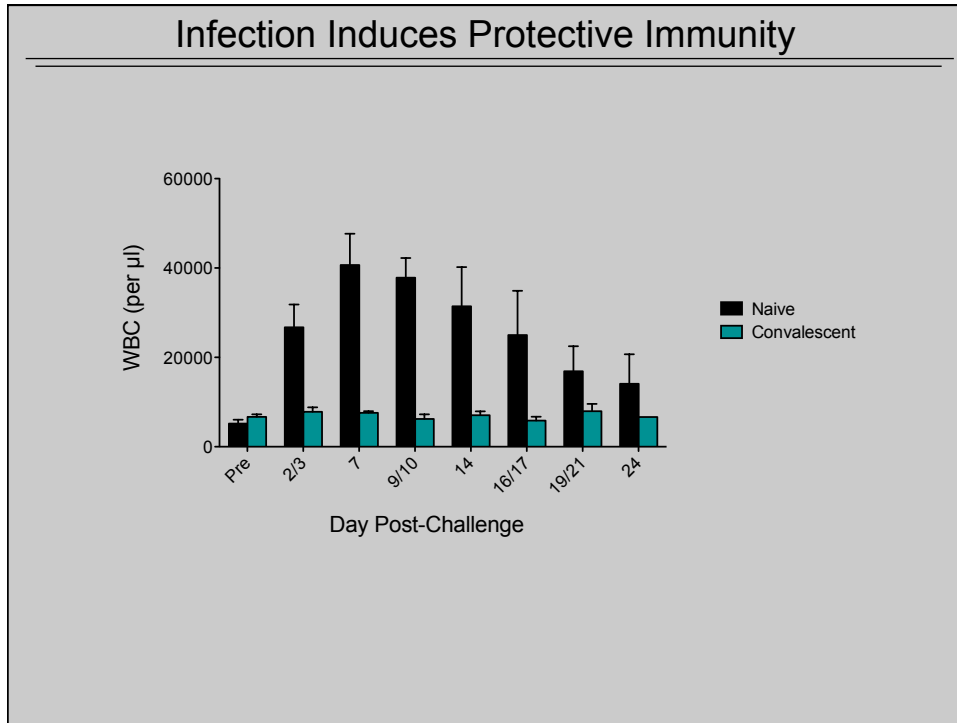


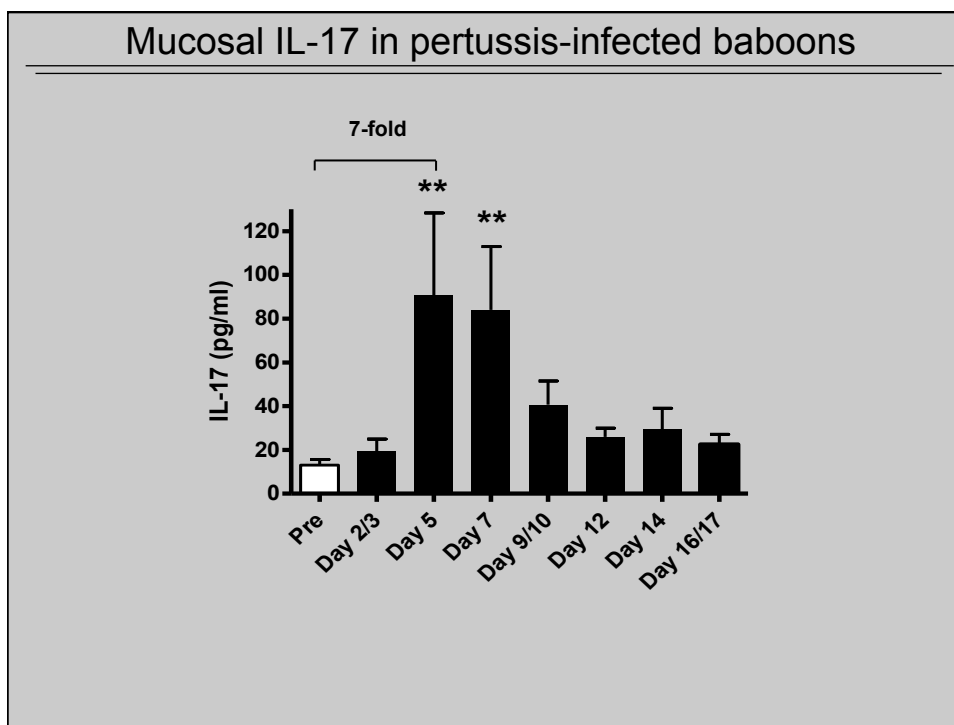
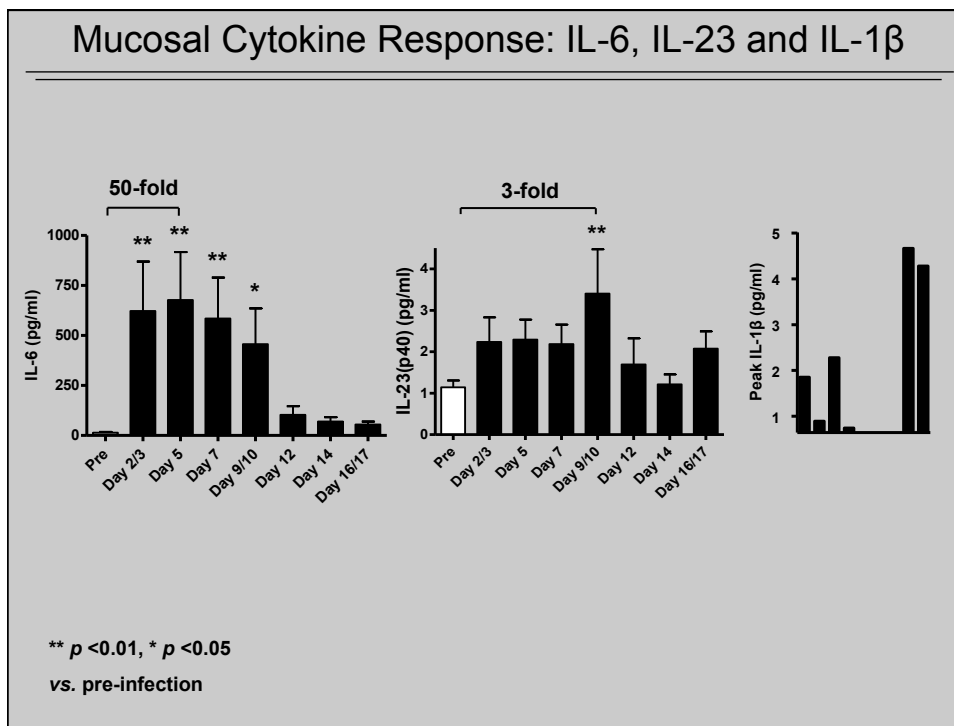


The Host Response to *B. pertussis* Infection

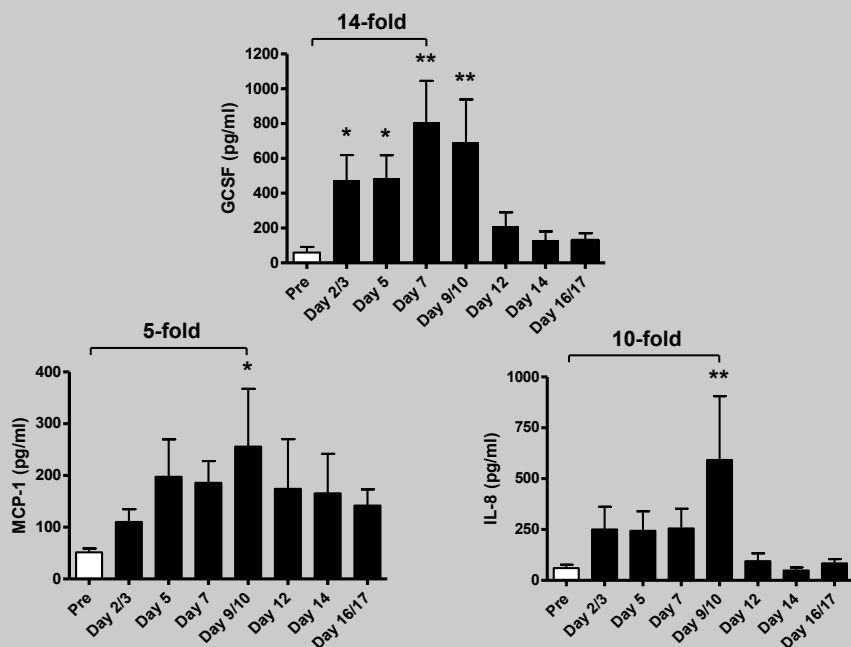
Infection Induces Anti-*B. pertussis* Humoral Responses



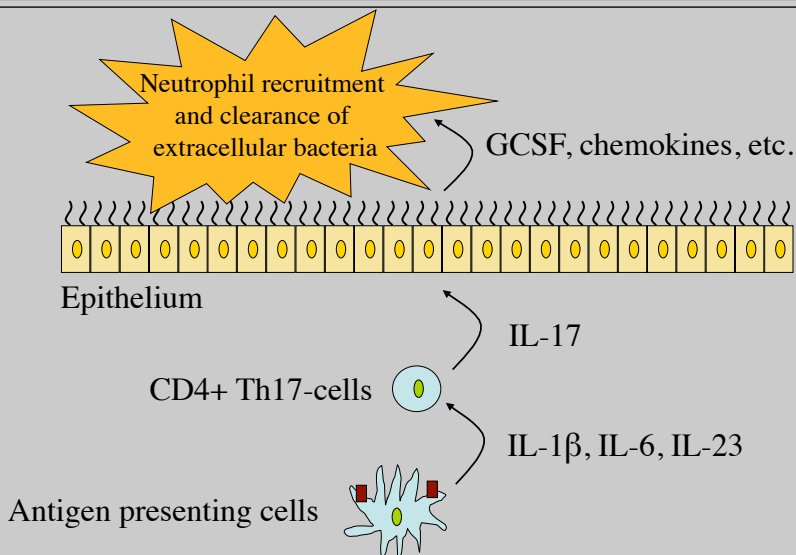




Mucosal expression of IL-17 effector chemokines and cytokines

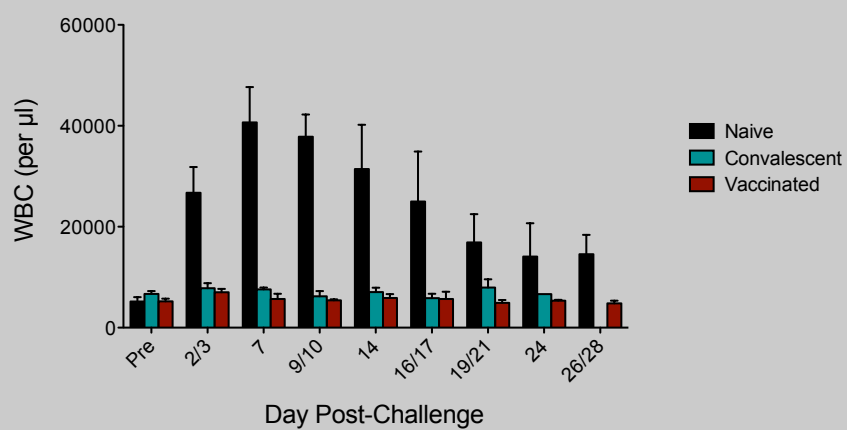


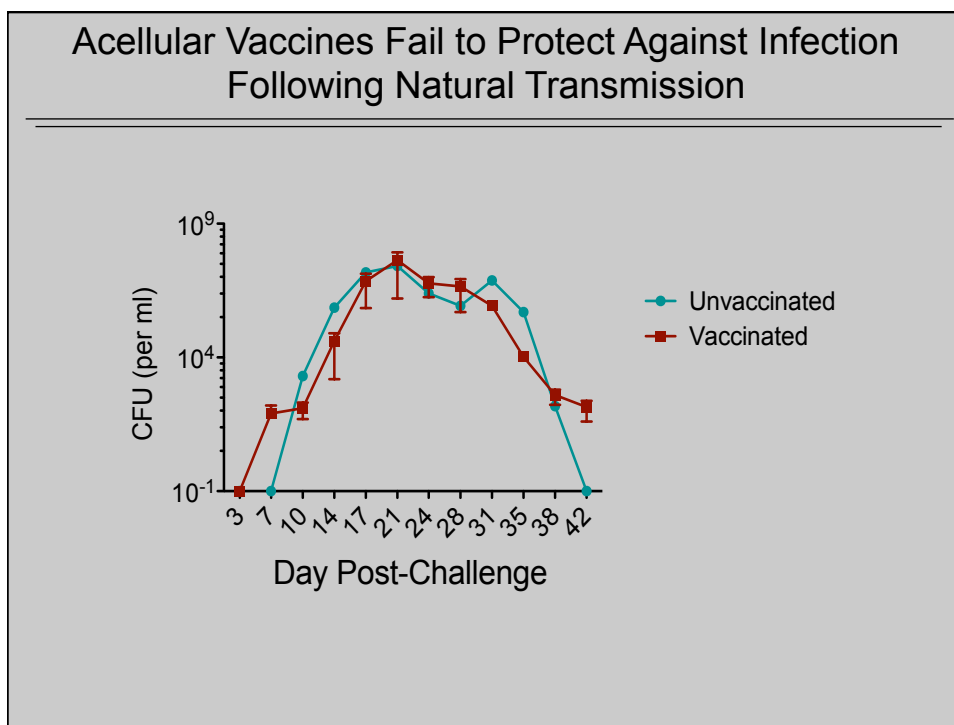
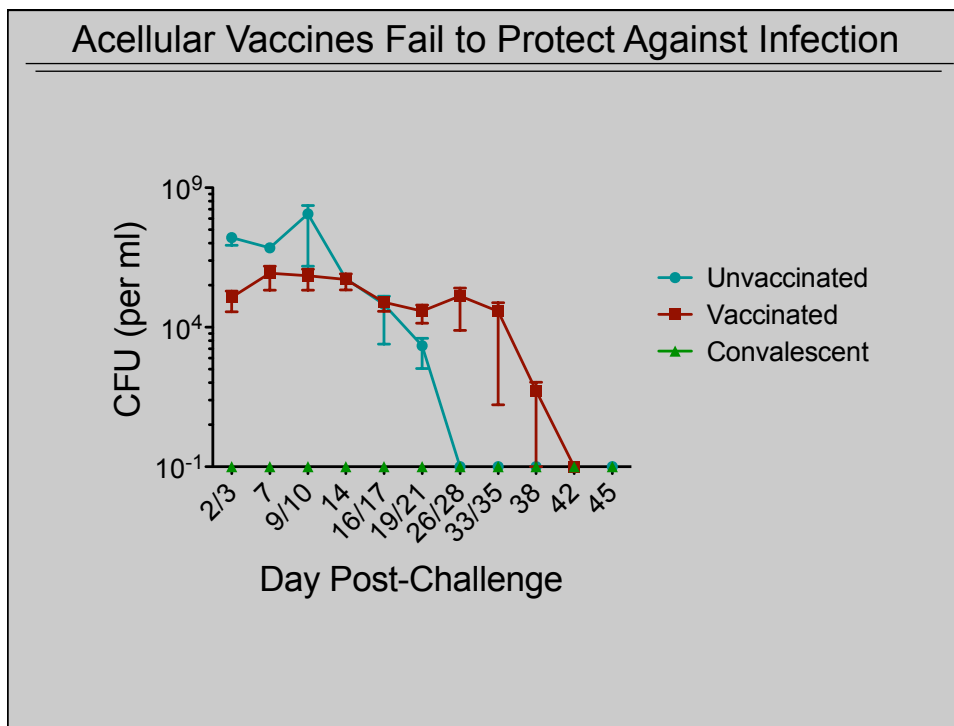
Th17 immune responses are involved in the clearance of extracellular bacteria

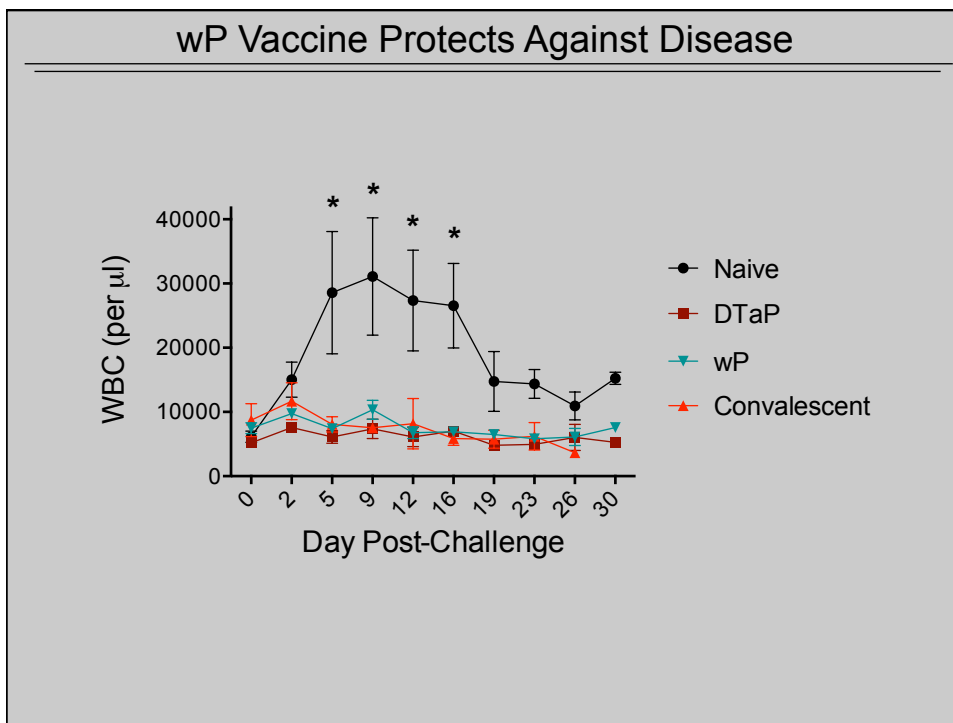
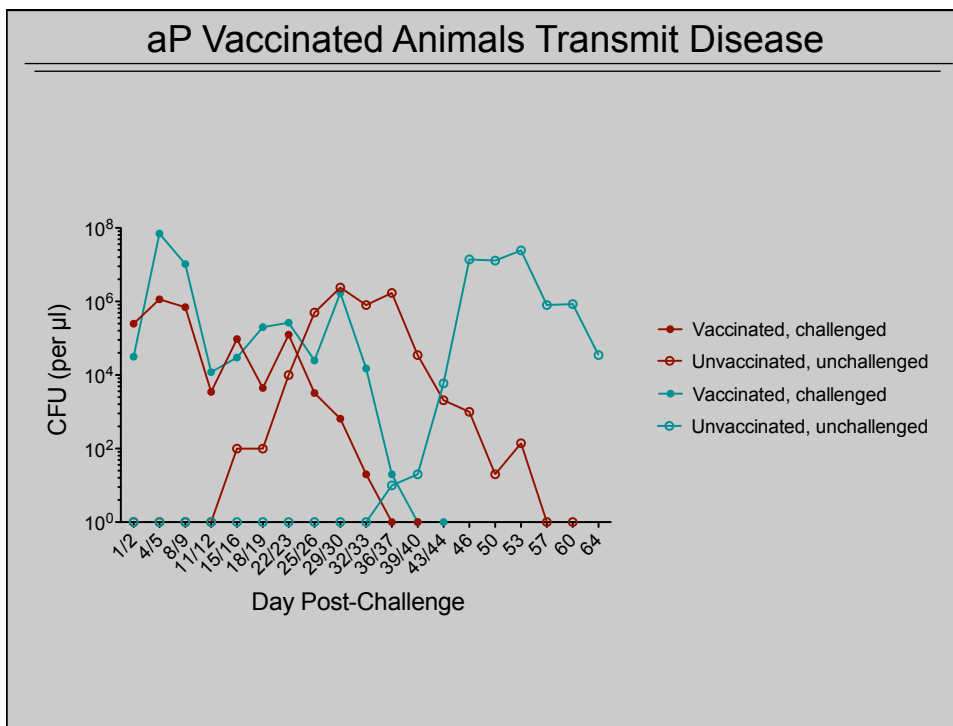


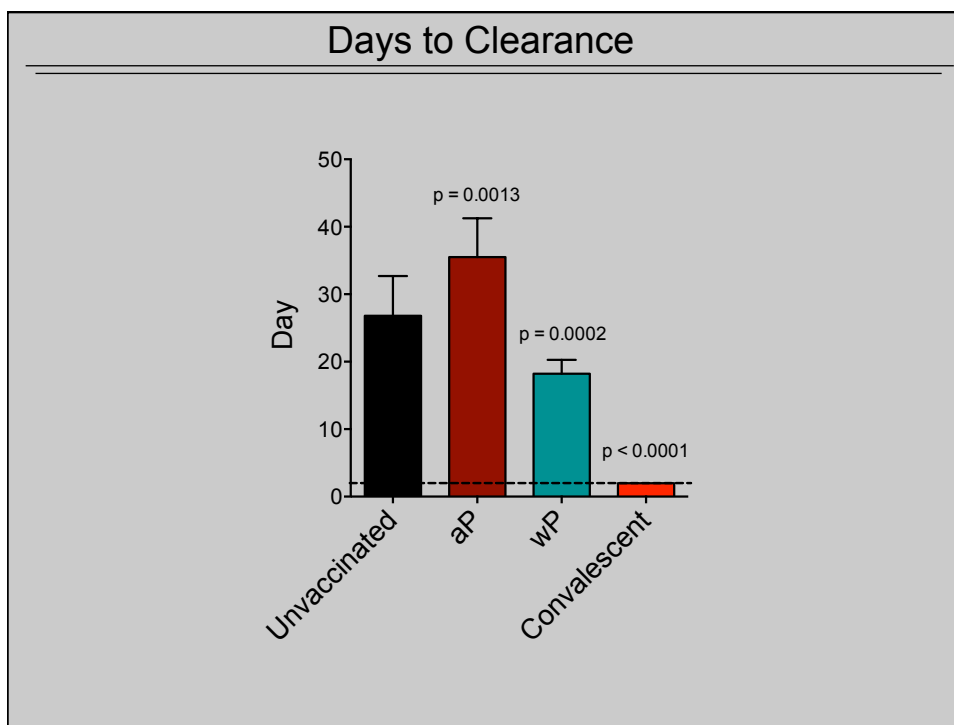
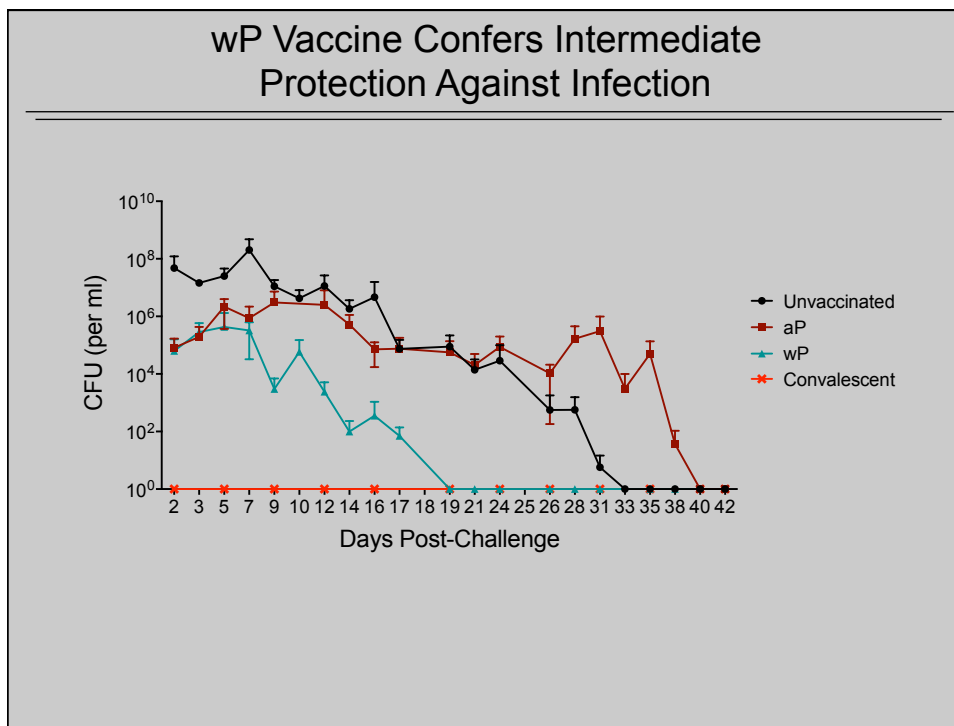
Evaluation of Pertussis Vaccines Using the Baboon Model

Acellular Vaccines Protect Against Disease

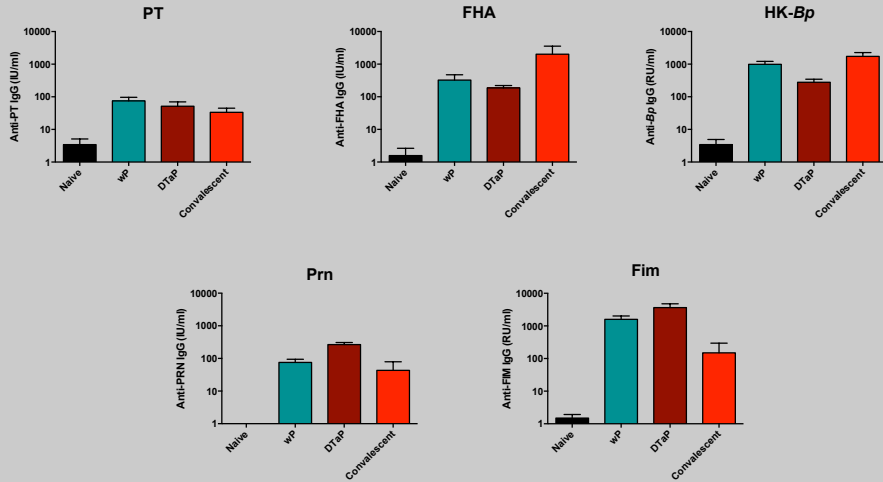




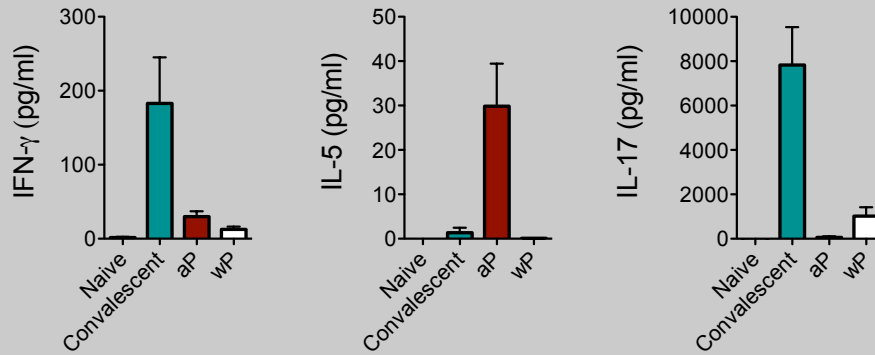




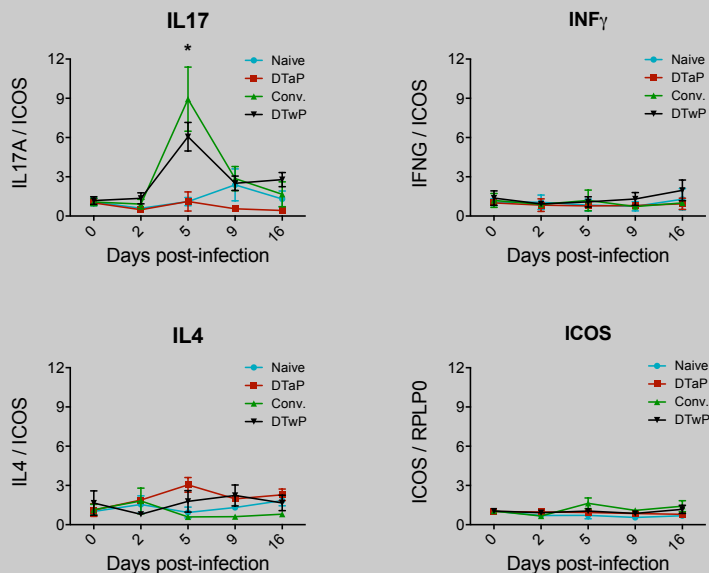
Both aP and wP Induce High Antibody Titers



Exposure Determines Skewing of Adaptive Response



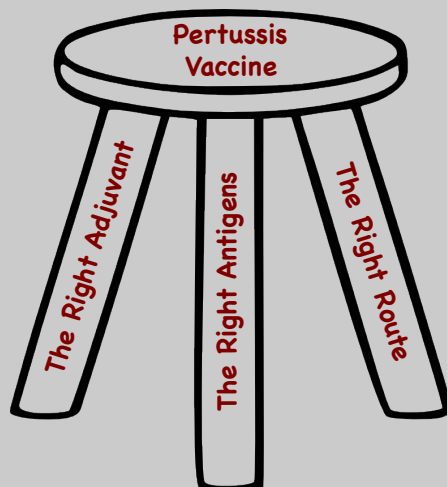
wP Vaccine Induces Th17 Response *In vivo*



Summary of Host Response Studies

- ❖ Th2-mediated antibody response to acellular vaccination prevents symptoms but not infection, carriage or transmission.
- ❖ These data suggest that acellular-vaccinated individuals might act as a reservoir for *B. pertussis* circulation.
- ❖ Infection and whole-cell vaccination induce Th17 memory and protect from colonization.
- ❖ Hypothesis: To prevent *B. pertussis* colonization you need Th17 immunity and opsonizing antibodies.

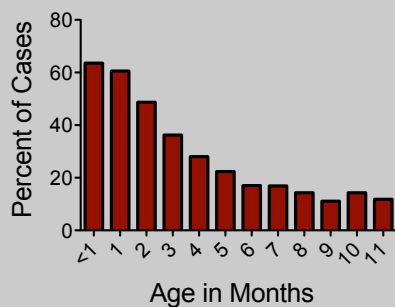
Next Generation Pertussis Vaccine



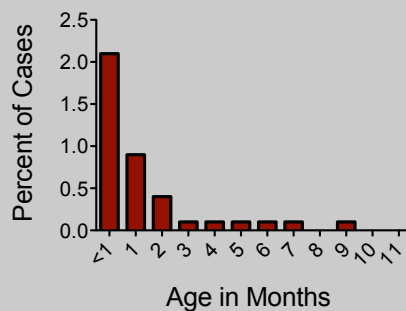
Protecting Newborns

Severity of Disease in Infants

Hospitalizations



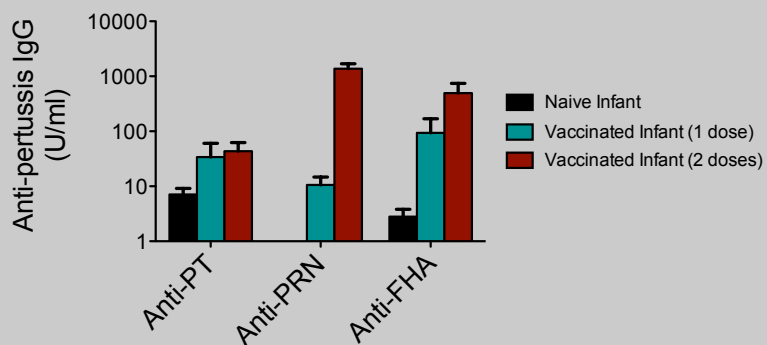
Deaths



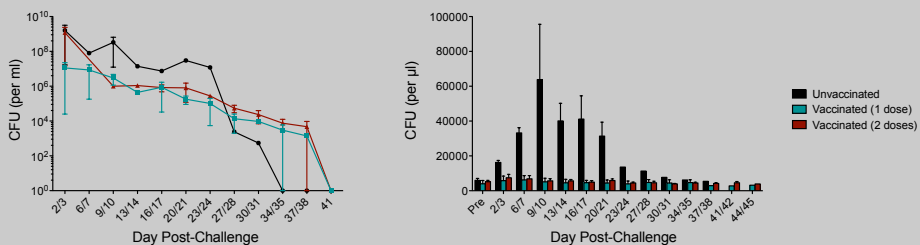
Proposed Strategies to Protect Newborns

- ❖ **Boosting of Adolescent Population**
Reduction of incidence in adolescents did not impact incidence in infants. Very little contact between adolescents and infants.
- ❖ **Cocooning**
Difficult to implement. Due to incomplete protection from transmission, cocooning is likely to be less effective than hoped.
- ❖ **Neonatal Vaccination**
aP vaccination at birth. Confers elevated titers early but still leaves window of vulnerability in first 2-3 weeks. Effectiveness unknown.
- ❖ **Maternal Vaccination**
aP-primed mothers are boosted during 3rd trimester. Infants have elevated titers from birth. Effectiveness unknown.

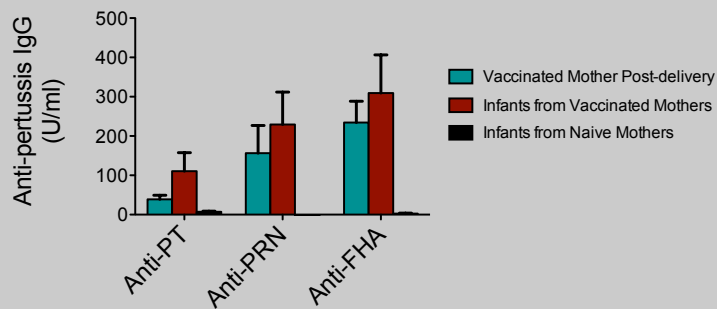
Vaccination of Neonates Induces IgG Response



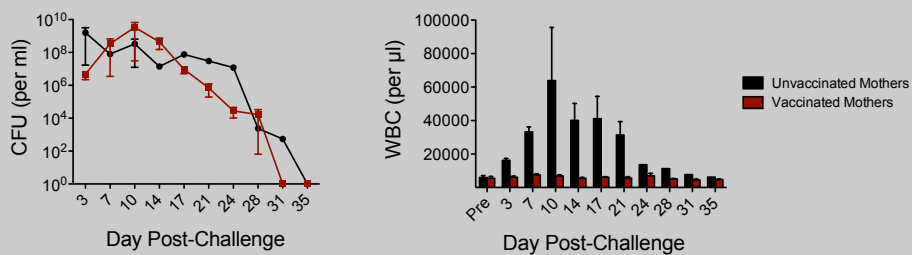
Neonatal Vaccination Confers Protection



Trans-placental transfer of Maternal IgG



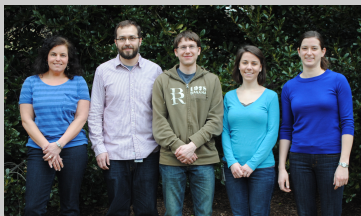
Maternal Vaccination Confers Protection



Summary of Infant Challenge Studies

- ❖ These studies provide proof-of-concept that neonatal and maternal vaccination may prevent severe pertussis in infants.
- ❖ Trans-placental transfer of maternal antibodies was sufficient to prevent severe pertussis. This is consistent with our interpretation that protection from acellular pertussis vaccination is primarily antibody-mediated.

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